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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/676,734	09/29/2000	Charles Joel Arntzen	P00245US D	1914

7590 08/13/2003

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	14

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/676,734	ARNTZEN ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-75,83,84,88,91 and 98-100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-75,83,84,88,91 and 98-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 20, 2003 has been entered.

Claims 73, 83, 84, 88, 98 and 100 are currently amended.

Claims 1-72, 76-82, 85-87, 89-90 and 92-97 are cancelled.

Claims 73-75, 83-84, 88, 91 and 98-100 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claims 83-84 and 98 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the transgenic plants expressing the specific animal viral antigens at the levels set forth in Applicant's working examples, does not reasonably provide enablement for expressing in any plant animal viral antigens at any level, or at levels recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope

with these claims, for the reasons of record set forth in the office action mailed December 9, 2002.

Claim 98 remains rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transgenic plant tissue expressing a recombinant transmissible gastroenteritis virus (TGEV) S-protein or a recombinant hepatitis B surface antigen (HbsAg) protein, said tissue eliciting a mucosal immune response against transmissible gastroenteritis virus (TGEV) S-protein or hepatitis B surface antigen (HbsAg) protein upon oral administration to an animal, does not reasonably provide enablement for transgenic plant tissue expressing any recombinant protein of any kind from any source, said tissue eliciting a mucosal immune response against any animal viral protein upon oral administration to an animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants' arguments filed May 20, 2003, have been fully considered but they are not persuasive.

Applicants point to the submitted declaration of Dr. John Howard supporting the generation of an immune response in an animal upon exposure to transgenic plants expressing a viral antigen. Applicants additionally point to the submitted publication of Wigdorovitz et al. (Virology, 1999, Vol. 225, pages 347-353) showing the induction of a protective antibody response in animals fed transgenic plants expressing a viral antigen. Applicants further point to

the submitted reference of Kapusta et al. (FASEB J., 1999, Vol. 13, pages 1796-1799) showing that mice fed transgenic lupin expressing hepatitis B virus surface antigen developed significant levels of anti-HbsAg antibodies (reply pages 8-9).

The Office acknowledges the declaration of Dr. John Howard and the submitted publications of Wigdorovitz et al. (Virology, 1999, Vol. 225, pages 347-353) and Kapusta et al. (FASEB J., 1999, Vol. 13, pages 1796-1799), and claim 98 no longer stands rejected for lack of enablement. The Office maintains, however, that the full scope of claim 98 is not enabled. Claim 98 is currently directed to plant tissue "expressing a recombinant protein" at a level that will elicit a mucosal immune response "against an animal viral antigen" upon oral administration to an animal. That plant tissue expressing any recombinant protein of any structure and any function obtained from any source would elicit a mucosal immune response against any animal viral antigen upon oral administration to an animal is unpredictable. First, not all recombinant proteins would necessarily elicit a mucosal immune response upon oral administration to an animal, as not all recombinant proteins would be recognized as antigenic by the animal. Second, a mucosal immune response against an animal viral antigen would not be elicited by any recombinant protein of any structure and any function obtained from any source, as immune responses are known to be specific for the antigen administered.

Applicants also point to page 24 of the specification as disclosing how to make transgenic plants that express a viral antigen protein at levels of 0.03% or more of total soluble protein, 0.05% or more of total soluble protein, or 0.1% or more of total soluble protein. Applicants further point to pages 8-9, 15, 20 and 29 of the specification as disclosing the type of vector to be

used, the type of animal viral protein to be expressed, the types of plants to be transformed, the level at which the recombinant protein must be expressed in order to elicit an immune response, and the manner in which the tissue should be administered, and argue that the specification enables the claimed invention (reply pages 9-10).

The Office acknowledges the teachings at pages 8-9, 15, 20, 24 and 29 of the specification, and the scope of the enablement rejection has been adjusted accordingly, but the Office maintains that the full scope of the claimed invention is not enabled, as the level of expression of a recombinant protein in transgenic plants is unpredictable. The level of expression of a recombinant protein in transgenic plants is unpredictable because the level of expression is affected by multiple variables, variables which include but are not limited to the type of promoter and terminator used in the expression vector, the plant species transformed by the expression vector, the type of tissue in which the protein is expressed, the stability of the mRNA transcribed from the recombinant protein coding sequence, the translation efficiency of the mRNA transcribed from the recombinant protein coding sequence, and the stability of the recombinant protein. Accordingly, different levels of expression would be expected for different types of recombinant proteins, or for the same protein expressed from different types of expression vectors, or for the same protein expressed in different species or in different tissues. The specification does not provide sufficient guidance for one skilled in the art to express at the claimed levels, without undue experimentation, any recombinant animal viral antigen protein using any type of expression vector in any species of plant or in any plant tissue, as the specification discloses the expression at the claimed levels of only one recombinant animal viral

antigen protein in two plant species and two plant tissues using only two different types of expression vectors.

Claim 88 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 88 is indefinite in the recitation of "wherein said plant tissue is administered orally". The meaning of the phrase is unclear, as the claim recites no indirect object indicating to whom or for whom or for what the administration of plant tissue is performed.

Claim 98 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 98 is indefinite in the recitation of "expressing a recombinant protein". It is unclear how plant tissue "expressing a recombinant protein" would elicit a mucosal immune response against "an animal viral antigen", as immune responses are antigen specific. It is suggested that the claim be amended to indicate that the recombinant protein is a recombinant animal viral antigen protein.

Claim 99 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 99 is indefinite in the recitation of "which triggers the production of antibodies". First, it is unclear from the claim language what triggers the production of

antibodies, the plant or the viral antigen? Second, it is unclear where or in what context the production of antibodies occurs, as the claim recites no context or location.

Claim 99 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 99 is indefinite in the recitation of "which is derived from a hepatitis B surface antigen or transmissible gastroenteritis virus spike protein". It is unclear from the claim language what is derived from a hepatitis B surface antigen or transmissible gastroenteritis virus spike protein, the viral antigen or the antibodies?

Claim 99 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 99 is indefinite in the recitation of "derived". It is unclear what aspects of the hepatitis B virus surface antigen or transmissible gastroenteritis virus spike protein are derived by the viral antigen or antibodies and which aspects are retained by the hepatitis B virus surface antigen or transmissible gastroenteritis virus spike protein. It is suggested that the claim be amended to recite "obtained" rather than "derived".

Claim 100 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 100 is indefinite in the recitation of "which triggers a mucosal response to a viral protein". First, it is unclear from the claim language what triggers the mucosal immune

response, the plant or the protein? Second, it is unclear where or in what context the mucosal immune response occurs, as the claim recites no context or location. Third, it is unclear how a plant comprising "a protein" would trigger a mucosal immune response to "a viral protein", as immune responses are antigen specific.

Claim 100 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 100 is indefinite in the recitation of "plant part, or a crude plant extract". First, it is unclear how a transgenic "plant" may be in the form of a "plant part" or "crude plant extract", as a "plant" is not equivalent to a "plant part" or "crude plant extract". Second, it is unclear in what way the plant extract is "crude", as those skilled in the art define "crude extract" differently.

Claim Rejections - 35 USC § 102

Claims 73-75, 88, 91 and 98-100 are rejected under 35 U.S.C. 102(e) as being anticipated by Goodman et al. (U.S. Patent 4,956,282, issued September 11, 1990), for the reasons of record set forth in the office action mailed December 9, 2002.

Applicants' arguments filed May 20, 2003, have been fully considered but they are not persuasive.

Applicants argue that the antigen viral properties of the antigen viral proteins disclosed by Goodman are not inherent to the proteins, and that the Examiner has failed to establish by fact or technical reasoning that the antigenic property of the animal viral protein disclosed by

Goodman is inherent. Applicant further argues that it is not a given among those skilled in the art that animals will always have an antigenic response to the oral administration of plant tissue per se, and the examiner has failed to recite a source for this statement. Applicants point out that plant tissue in the form of feed is regularly administered to animals on a regular basis, and applicants are unaware of an antigenic response being a given accepted fact. Applicants further point out that Goodman does not provide that a viral antigen can be expressed in a plant and cause a mucosal immunogenic response. Applicants argue that the amendment of claims 73-75, 88, 91 and 99-100 render the rejection moot (reply pages 10-11).

With respect to the inherency of the antigenicity of viral proteins, the Office maintains that, absent evidence to the contrary, the antigenicity of the expressed protein is considered to be an inherent property of the protein itself, as it is well known in the art that protein antigenicity is mediated by epitopes comprising specific amino acid residues of the protein. In this regard, Applicant has provided no evidentiary support as to why the viral antigens of Goodman would not elicit an immune response. It is evident that Goodman intended for the expressed viral antigens to cause an immune response, as Goodman et al. teaches the expression in plant cells of mammalian proteins, including antigens associated with animal viral pathogens, that retain their physiological activity (abstract; column 1 lines 39-45 and 64-67; column 3 line 12 and line 31). It is unclear why Applicant believes that the viral antigens taught by Goodman would not elicit an immune response. Goodman also teaches oral administration of transgenic plants expressing physiologically active mammalian proteins (column 5 lines 51-60).

With respect to Applicants' argument that it is not a given among those skilled in the art that animals will always have an antigenic response to the oral administration of plant tissue per se, the Office maintains that the issue of animals having an antigenic response to the oral administration of plant tissue per se is no longer germane to the instant rejection, as amended claim 88 is no longer directed to plant tissue that elicits an unspecified antigenic response, and the remaining pending claims indicate that it is the expressed recombinant animal viral antigen protein that is capable of inducing the immune response (claims 73-75 and 91), or that a mucosal immune response is elicited against an animal viral antigen (claim 98), or that the plant comprises a viral antigen which triggers production of antibodies (claim 99), or that the plant comprises a protein which triggers a mucosal immune response to a viral protein (claim 100) .

With respect to the argument that Goodman does not provide that a viral antigen can be expressed in a plant and cause a mucosal immunogenic response, the Office maintains that the rejected claims do not require that a viral antigen can be expressed in a plant and cause a mucosal immunogenic response. Claim 73 as amended requires only that the transgenic plant express a protein that is capable of inducing a mucosal immune response when administered to a human or animal. The Office maintains that the capacity of inducing a mucosal immune response when administered to a human or animal is an inherent property of the protein, regardless of the system in which it is expressed. Claim 88 requires only that the transgenic plant of claim 73 comprise plant tissue administered orally. The Office maintains that the capacity to be orally administered is an inherent property of the plant tissue. Claim 100 as amended requires only that the plant comprise a protein which triggers a mucosal immune response. The Office maintains

that the capacity to trigger a mucosal immune response is an inherent property of the protein, regardless of the system in which it is expressed.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
August 11, 2003

Phuong Bui 8/11/03
PHUONG T. BUI
PRIMARY EXAMINER